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14. ABSTRACT

The objective of this project is to develop an NF1-specific health-related quality of life (HRQL) instrument for use with pediatric patients. Semi-structured interviews with children with NF1, their parents, and teachers were used to derive important domains and item content, and the first-generation instrument was developed. This instrument has undergone an initial examination of its psychometric properties and the content was revised accordingly. Following this initial field trial, the second generation instrument will be tested administered in a battery of measures to further assess its reliability and validity as well as its applicability in a clinical trials setting. At the conclusion of this third year, we have completed all interviews, transcribed all interviews, and reviewed them for content. This content review was then used to develop the first-generation instrument. The instrument was completed by 83 children with NF1 and 83 parents of children with NF1. The resulting responses have been analyzed for internal consistency and feasibility. The instrument demonstrated acceptable internal consistency (coefficient *alpha*) and was not perceived as either difficult or upsetting to complete. In the final stage of the project, the revised instrument will be completed on multiple occasions, and further tests of the reliability and validity will be completed.

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Annual Report Year 3
(August 2005)

11. INTRODUCTION

The objective of this project is to develop an NF1-specific health-related quality of life (HRQL) instrument for pediatric patients and their parents. Semi-structured interviews with children with NF1, their parents, and teachers yielded relevant domains and content that were used to develop the first-generation instrument. This first-generation instrument was field tested for psychometric properties and understandability and then revised. The revised instrument will be completed by a group of children and their parents to test its validity and sensitivity to change in clinical status. It is our hypothesis that the addition of this disease-specific measure will significantly improve the descriptiveness and quantification of the impact of NF1 and its treatment on children's lives.

2. BODY

The original Statement of Work identified the following tasks:

Task 1: Identify domains and items to reflect important aspects of HRQL (COMPLETED)
- Complete review of literature to gather previously identified HRQL topics
- Develop standardized interviews for patients, parents, teachers, and health care professionals
- Pilot interviews and modify as needed
- Conduct interviews of patients, parents, teachers and health care professionals
- Transcribe interviews, review for functioning areas impacted by NF1

Task 2: Administer preliminary items to sample of NF1 patients and parents and use item analysis methods to construct preliminary HRQL instrument.
- Recruit NF1 participants and parents
- Mail out questionnaires for completion and return
- Enter and analyze data
- Produce final NF1-specific instrument for studies in subsequent tasks

Task 3: Conduct reliability, validity and responsivity studies for NF1 instrument (IN PROGRESS

Additionally, although not stated in the original Statement of Work, we were required to gain approval from both the Army/Department of Defense Human Subjects Review Board and our local Institutional Review Board prior to recruiting participants. Because of the manner in which the projects were proposed, and the reliance on material/questionnaires developed at each stage, it was necessary to submit separate Human Subjects protocols for each of the 3 projects (interviews, first-generation validation, and final version validation).

Status of Work. As noted in prior reports, Task 1 has been completed. Each of the tasks in Task 2 will be listed again, with the current status described:

Task 2: Administer preliminary items to sample of NF1 patients and parents and use item analysis methods to construct preliminary HRQL instrument

- *Recruit NF1 participants and parents.* Since the last annual report, we successfully recruited 83 children with NF1 between the ages of 8 and 17 years, and 83 parents of children with NF1 to complete the first generation health-related quality of life instrument (developed in Task 1).

- *Mail out questionnaires for completion and return.* We have received 83 completed questionnaire packets from children with NF1 and 83 completed questionnaire packets from parents of children with NF1.

- *Enter and analyze data.* All data from children and parents have been entered into SPSS v13 for statistical analysis. This includes parent and child responses to the HRQL instrument, ratings of disease severity, and demographic information.

- *Produce final NF1-specific instrument for studies in subsequent tasks.* The revised version of the NF1-specific HRQL instrument has been prepared based on information and comments collected in this task. This version will be used to complete Task 3.

Task 3: Conduct reliability, validity and responsivity studies for NF1 instrument

This task is currently in progress, as we secure approval from both the West Virginia University Institutional Review Board and the Department of Defense Human Subjects Review Board.

Because of the delays we have experienced (largely Review Board approvals), we requested and were granted a one-year no cost extension to complete Task 3.

Results and Discussion of Research Activities. The primary findings from the current activities relate primarily to the descriptiveness, understandability, and general psychometric properties of the first generation NF1-specific HRQL instrument. Parents and children completed parallel versions of the instrument, which were identical with the exception of wording ("I have....." vs. "my child has...").

Subjects. We recruited 83 children with NF1 between the ages of 8 and 17 years, and 83 parents of children with NF1 to complete the questionnaire, for a total of 166 participants. We recruited 40 males and 40 females participating (3 participants did not identify gender). Adult ratings of disease severity indicated that the majority of the sample fell into the mild range of severity (Riccardi scale) and the mild range of visible

impact (Ablon scale), suggesting that while there was a wide range of severity in our sample, as a group were mildly affected.

Missing Data, Clarity, Burden and Descriptiveness. Because part of our interest in the feasibility of employing an instrument such as this, we were interested in a number of related variables, including missing data (perhaps reflective of poor wording or a difficult to understand question), as well as informant-completed ratings of burden associated with completing the questionnaire and overall descriptiveness of the questions in terms of that individual's health-related quality of life. For child informants, there were minimal missing data (<3%), <1%% of responses that for which the informant indicated that the question was not clear, and the average rating of burden associated with completing the instrument was minimal, with mean difficulty ratings of 4.3 and 4.5 (child and parent, respectively), and mean upset ratings of 4.3 and 4.6 (child and parent, respectively) out of 5 (5 = not at all). For adult informants, there were minimal missing data (<3%), <1% of responses that for which the informant indicated that the question was not clear, and the average rating of burden associated with completing the instrument was minimal. Both parent and child informants rated the item content as "good" in terms of how descriptive these items were of the child's overall health-related quality of life. However, it should be noted that child informants did require some degree of assistance, with 67% reporting help from an adult (mother or father).

General Psychometric Properties. For the purposes of this task, we examined the psychometric properties of the first generation instrument by examining the descriptive statistics of the items and subscales (dispersion, central tendency) and the internal validity of the subscales (Cronbach's *alpha*). Other important properties, such as test-retest reliability and various forms of validity, are the focus of Task 3.

Descriptive statistics. Descriptive statistics for each item are presented in Table 2 for both parents and children. As can be seen, the majority of items yielded a range of responses from both groups of informants.

Internal validity. The internal validity of a scale measures the extent to which the items are measuring a uniform construct or domain, such as social functioning or behavior problems. Table 1 below presents the *alpha* coefficients for each subscale of the instrument. In general, these data suggest that the scale demonstrates satisfactory internal consistency/reliability.

TABLE 1: Cofficient *alpha* (Internal Consistency) for each subscale by informant.

Subscale	# of Items	Parent Informant	Child Informant
Appetite and Sleep	4	.583	.388
Pain	8	.866	.802
Understanding	2	.621	.619
Sensation	3	.421	.458
Symptoms	12	.847	.865
Psych and Behavior	25	.886	.856
School & Cognition	17	.957	.920

Social Relations	10	.805	.816
Appearance	10	.927	.882
Speech & Language	2	.585	.714

Table 2: Child and Parent Informant Mean Ratings for Each Item.

Item Descriptor	Item Code	Child Mean	Parent Mean
In general my health is.	GH1	4.01	3.76
Compared to this time last year my health is	GH2	3.80	3.57
Sick more easily than other kids	GH3	3.81	3.93
Had difficulty falling asleep/staying asleep	AS1	3.22	3.29
Had bad dream	AS2	4.22	4.22
Been less hungry	AS3	3.95	3.98
Been hungrier	AS4	3.62	3.79
Bothered that didn't know enough about NF	U1	4.25	4.55
Frustrated about having NF	U2	3.69	3.70
Had difficulty hearing others	SE1	4.31	4.41
Wears hearing aide	SEHA	0	0.05
Had trouble seeing	SE2	4.13	4.09
Wears glasses/contacts	SEGC	0.31	0.3
Had trouble feeling things	SE3	4.81	4.80
Hurt a lot	P1	3.94	3.90
Had muscle pains	P2	3.78	3.61
Had headaches	P3	3.59	3.57
Has stomachaches	P4	3.65	3.72
Had pain in bones or joints	P5	4.05	3.85
Had neurofibromas or other areas hurt to touch	P6	4.36	4.17
Compared to others my age the amount of pain is	P7	3.04	2.58
Pain keeps me from doing things want to do	P8	4.03	4.06
Felt sick to stomach	SY1	3.84	3.88
Had a headache	SY2	3.70	3.52
Had stomachache	SY3	3.72	3.71
Had a hard time breathing	SY4	4.53	4.59
Felt dizzy	SY5	4.23	4.65
Felt weak	SY6	4.23	4.47
Felt tired or fatigued	SY7	3.33	3.48
Had a hard time swallowing	SY8	4.58	4.76

Had a hard time keeping balance	SY9	4.25	4.30
Had difficulty tying shoes, using scissors	SY10	4.39	4.10
Been clumsy	SY11	4.03	3.62
Had a hard time riding a bike	SY12	3.89	3.72
Felt cranky	PB1	3.37	3.13
Worried	PB2	3.62	3.53
Anxious	PB3	3.62	3.54
Gotten easily frustrated	PB4	2.90	2.93
Gotten in trouble because of behavior @ school	PB5	4.35	4.09
Gotten in trouble because of behavior @ home	PB6	3.48	3.45
Felt afraid/scared	PB7	4.01	3.95
Felt sad, down or depressed	PB8	3.85	3.78
Felt angry	PB9	3.51	3.33
Worried about what might happen to me	PB10	3.85	3.90
Felt like crying	PB11	4.02	3.95
Felt lonely	PB12	3.95	3.98
Felt cheerful	PB13	2.14	2.44
Felt confident	PB14	2.32	2.61
Enjoyed things	PB15	1.90	2.19
Had fun	PB16	1.77	2.16
Felt jittery or restless	PB17	3.47	3.76
Argued	PB18	3.04	2.81
Wanted to be alone	PB19	3.59	3.54
Had mood swings	PB20	3.49	3.08
Not done what was asked	PB21	3.68	3.31
Had anxiety or panic attacks	PB22	4.61	4.6
Hit or kicked someone	PB23	4.14	4.11
Heard voices that weren't there	PB24	4.65	4.93
Compared to others, behavior is	PB25	3.69	3.34
Missed school because of health	SC1	4.21	4.36
School on vacation	SC1A	1	1
Been bothered because missed school	SC2	4.41	4.38
Hasn't missed any school	SC2A	1	1
Missed school to go to doctor or hospital	SC3	4.08	4.01
Had difficulty solving math	SC4	3.40	2.87
Had difficulty writing papers or reports	SC5	3.52	2.52
Had trouble following or	SC6	3.69	2.96

understanding directions			
Had difficulty remembering what read	SC7	3.45	2.88
Had trouble reading	SC8	3.87	3.16
Forgotten things	SC9	3.56	3.02
Had trouble keeping up with schoolwork	SC10	3.70	2.95
Had trouble turning schoolwork in on time	SC11	3.90	3.29
Had difficulty paying attention and concentrating	SC12	3.66	3.05
Had trouble writing neatly	SC13	3.11	2.38
Had a hard time sitting still in class	SC14	3.76	3.35
Had trouble organizing work or things	SC15	3.55	2.70
Had trouble spelling	SC16	3.43	2.71
How would you rate your ability to do schoolwork	SC17	3.70	2.96
Had trouble getting along with other kids	SR1	4.15	3.88
Helped others *****	SR2	2.32	2.43
Preferred to be alone	SR3	3.63	3.59
Preferred quiet activities	SR4	3.53	3.22
Avoided doing things with other kids	SR5	4.17	3.95
Felt bothered because couldn't do activities liked	SR6	3.56	3.56
Felt like other kids didn't want to do things with them	SR7	3.61	3.46
Felt like other kids didn't' want to be friend	SR8	3.9	3.38
How would you rate your family's ability to get along	SR9	3.80	3.83
How would you rate your ability to get along w/others	SR10	4.04	3.60
Been teased about how look	A1	4.07	3.94
Felt bad about appearance	A2	3.94	3.93
Worried about looks	A3	3.95	3.79
Been teased about size	A4	4.21	3.86
Avoided doing things w/others because of looks	A5	4.53	4.45
Done things to hide part of body because of looks	A6	4.25	4.19
Noticed people staring	A7	4.33	4.17
Heard strangers make rude	A8	4.55	4.23

comments			
Worried about other people teasing them	A9	3.84	3.71
Am satisfied with looks	A10	3.73	3.54
People had hard time understanding me when talk	SL1	3.5	3.36
I had a hard time understanding what other people say	SL2	4.15	3.94
How well did questions describe quality of life	GR1	3.82	3.55
How would you rate your overall quality of life	GR2	3.9	3.78
How difficult was it to complete this survey	GR3	4.27	4.46
How upsetting was it to complete this survey	GR4	4.31	4.59

Overall, the data gathered in this phase indicate that we were able to include item content that was reliable and generally descriptive of children's health-related quality of life. Additionally, participants did not perceive the instrument as being burdensome or upsetting to complete. Several items which were difficult to a small number of participants to understand have been re-written for the revision of the instrument, which is now ready to field in the final study.

3. KEY RESEARCH ACCOMPLISHMENTS

The primary accomplishment during this period of reporting is the successful fielding of the first generation NF1-specific HRQL instrument. We have shown that the instrument demonstrates acceptable internal consistency, and that it can be completed with minimal difficulty and distress by respondents with diverse backgrounds, experiences, and disease severity.

4. REPORTABLE OUTCOMES AND CONCLUSIONS

Although the generalizability of these data has not been established, the participants in this study did provide potentially useful information regarding the perceptions of health and quality of life among children with NF1. For example, children's overall health was rated as good by both parents and children, although children perceived that they got sick more easily that others the same age. Children were typically described as cheerful and confident. There appears to be a trend toward children reporting more behavior problems than did parents, but these are clearly preliminary data. School problems and social difficulties were noted as well. While it is premature to draw firm conclusions or generalizations regarding children with NF1, these data do provide the opportunity for further hypothesis generation and testing.

5. REFERENCES

6. APPENDICES

None